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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,405	11/21/2001	Alan L. Mueller	50877.0030	4028

26582 7590 08/10/2006

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DENVER, CO 80201

EXAMINER
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KWON, BRIAN YONG S

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 08/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/990,405

Applicant(s)

MUELLER ET AL.

Examiner

Brian S. Kwon

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1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 5, 6 and 21-35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 5, 6 and 21-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

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## **DETAILED ACTION**

### ***Status of Application***

1. By Amendment filed June 27, 2006, claims 5 and 25-27 have been amended and claims 30-35 have been newly added. Claims 5-6 and 21-35 are currently pending for prosecution on the merits.

### ***Response to Arguments***

2. Applicant's arguments with respect to claims 5-6 and 21-29 have been considered but are moot in view of the new ground(s) of rejection.

### ***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

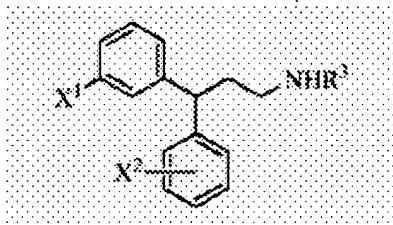
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 5-6 and 21-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mueller et al. (WO 96/40097) in view of Skolnick et al. (Pharmacopsychiatry, abstract, 1996 January, 29:1, 23-6).

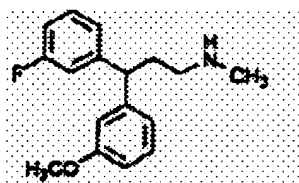
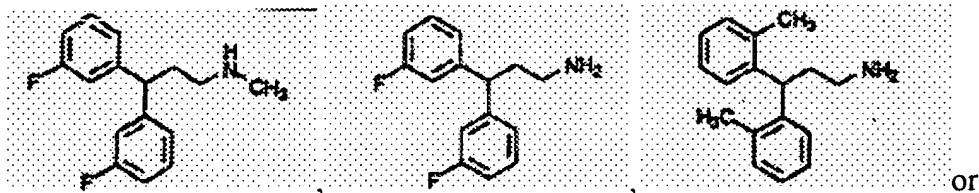
The claims read on a method of treating a patient for depression comprising a compound



of the formula

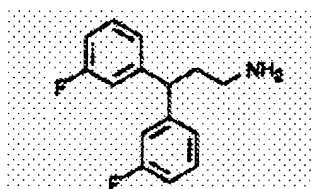
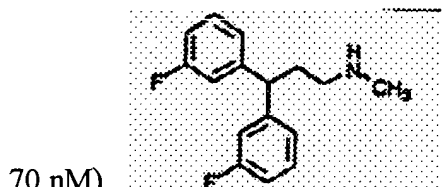
Further limitation includes "X¹ is -F, -Cl, -OCF₃ or -CF₃ and X² is either 2-OCH₃, 2-CH₃, 3-F, 3-CF₃, or 4-CF₃" (claim 6); "X¹ and X² are -F, and R³ is -H" (claim 21); "X² is at the 3-position" (claim 22); "X¹ and X² are -F, and R³ is -CH₃" (claim 23); "X² is at the 3-position" (claim 24); "the compound is active at a serotonin reuptake site and at a N-methyl-D-aspartate (NMDA) receptor" (claim 25); "the compound has an NMDA receptor IC₅₀ of about 50 nM to about 1 μM" (claim 26); "the compound has an NMDA receptor of IC₅₀ of about 100 nM to about 800 nM" (claim 27); and the compound of

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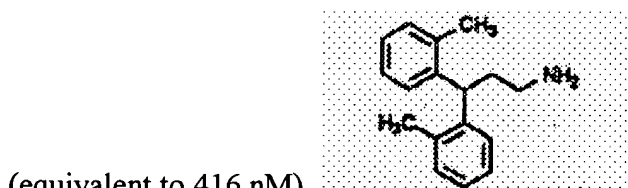


(claims 28-35) or pharmaceutically acceptable salts.

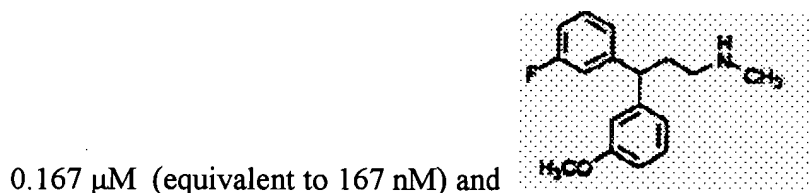
Mueller teaches arylalkylamine compounds represented by the formula or their pharmaceutically acceptable salt as a potent NMDA receptor antagonist, for example

(compound 20) having NMDA receptor  $IC_{50}$  of 0.070  $\mu$ M (equivalent to

70 nM),

(compound 60) having NMDA receptor  $IC_{50}$  of 0.416  $\mu$ M

(equivalent to 416 nM),

(compound 65) having NMDA receptor  $IC_{50}$  of0.167  $\mu$ M (equivalent to 167 nM) and

(compound 142), that is useful

for the treatment of neurological disorders including epilepsy, Alzheimer's disease, Parkinson's

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disease, and Huntington's disease (abstract; pages 24-25; pages 62-64; page 255, line 16 thru page 256, line 9; claims 1, 18, 19 and 77 and 80; Table 5-7 and 9). Mueller also discloses that said arylallylamine compounds do not have PCP-like psychotomimetic activity (page 122, lines 9-12; page 32, lines 3-10; page 96, lines 8-22) and have an  $IC_{50} \leq 10\mu M$  at NMDA receptor, more preferably  $\leq 2.5\mu M$ , and most preferably  $\leq 0.5\mu M$  (equivalent to 500 nM) at an NMDA receptor (page 50, lines 28-24 and claims 73-75); and shows activity at a serotonin reuptakes site and at a N-methyl-D-aspartate (NMDA) receptor (Table 10).

Skolnick provides links between NMDA receptor antagonist and the treatment of depression. Skolnick teaches that NMDA antagonist mimic the effects of clinically effective antidepressants in both preclinical tests predictive antidepressant action and procedures designed to model aspects of depressive symptomatology; and NMDA receptors is involved in the pathophysiology of depression (abstract).

The teaching of Mueller differs from the claimed invention in the use of the claimed compounds represented by the formula, namely the compound 20, 25, 60 and 142, for the treatment of depression. To incorporate such teaching into the teaching of Mueller, would have been obvious in view of Skolnick who teaches nexus between NMDA receptor antagonist and the treatment of depression.

One having ordinary skilled in the art at the time of the invention was made would have expected as taught by Skolnick that NMDA receptor mechanism is involved in pathophysiology of depression and the downregulation of NMDA receptor by NMDA antagonist would provide clinical utility in the treatment of depression. One having ordinary skill in the art would have been motivated to make the modification such that the adverse effect associated with inhibition

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of NMDA receptor mediated response (e.g., PCP-like psychotomimetic effect) would be greatly decreased by the administration of the claimed compound. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

With respect to the “the compound is active at a serotonin reuptake site and at a N-methyl-D-aspartate (NMDA) receptor” (claim 25), “the compound has an NMDA receptor  $IC_{50}$  of about 50 nM to about 1  $\mu$ M” (claim 26) and “the compound has an NMDA receptor of  $IC_{50}$  of about 100 nM to about 800 nM” (claim 27), as discussed in preceding comments, those characteristics or properties are deemed to be present in the referenced arylalkylamine analogs such as compound 20, 25, 60 and 142. Thus, the above references in combination makes obvious the instant invention.

### *Conclusion*

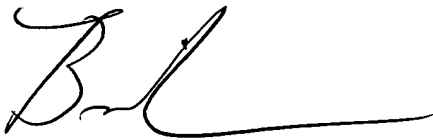
4. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Please reference Jones et al. (Journal of Medicinal Chemistry, 1971, Vol. 14, No. 2, pp. 161-164).
5. No Claim is allowed.
6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see <http://pair-direct.uspto.gov> Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon  
Patent Examiner  
AU 1614

A handwritten signature in black ink, appearing to be 'BK' followed by a long horizontal stroke.